

AGGGAGAGTCTGCCACAAAGTTTGATATTCCTCACTGAGGCATCTATTCAAGTTGGCAGCAGACA
CTGAGCAGAACGTAGCACGGCAATGCTGGTAGCAATGCCGTCCGGCCAGCACTCAGAAGACGGAGGCA
GGAGAACATAGCTCCAGTCAGCCTCTACAATATAGTCAGTTGAAGTCAGCCAGCTAGACAACA
TGGAGAGCCTGTGCCAAGCCACTGGTAAGCCGAATCTCAGTAGCAGAGAGCTGCCAGGGTGCCTA
CTGC:AAAAAAAAACCTCAAACAAACAGAAGTAGGGAGGTGTAAAATAAGTGTAGGGGGTGAATT
AGCTGATGTGGACTTCAAATAAGTTACCTTTAGATACTTAAATCAATAGCATAGACCTGAAAC
TGTCTATCAGAAAATGTGTCTATTCTGAGGAAGGAGTGCTAACGAGGTTCTGTGAGGGGGCCTGGCT
TTGAGAGGGTGTACCATCACATAAGACTCCTAAAAGCACATACTTTATAAATTCAACATGAGCTTAAAC
ATCTTCTTGTCAATTGCGACTGAGCATGGAGTCTTCGATGCTGACACCAATTCAACTGACCTACA
CTCACGGCCTGTTCAACCCAAGACATTGCCCATGGTCAATTCTGGTCTCACTTGTCTATTGG
CTGCTAGGCAATGGGCTGGTGTGGTAGCTGGCTAAAGATGAAGACGACCGTGAACACAGCTGGT
TCCTCCATCTCACCCCTGGCGATTCCTGCTGCCCTCCTGCCCTCCTGGCTCACCTGATTCT
CCAAGGACACTGCCCTATGGCTGTTCTGTGCAAACCTTATCCATCCATTATTCTCAACATGTT
GCCAGTGTCTCCCTGTTACTGCCATTAGCCTGGACCGATGTCAGTACATAAGCCAATCTGGTGC
AGAACATCGAAACGTGAGAACCGCTTCGCCATCTGTTGATGTCTGGTAGCCTTGTGATGTG
TGTGCCCGTATTGTATACCGTGATCTGTTCAATTGGACAATCGCAGTATATGTAGATATAATTGAT
TCCTCCAGGTCAATGATTATGGGACTACGTGACAAACTAAGTCTACCAAGAACGAAATTCTACTGATA
ACTCCACTGCTCAGCTAACGGACATATGAATGACAGGGTCACTCCCTGTCAGGCAAGGGATTA
CTTTGGACAGTTACCAACTGCCCTCCAGTCACAGCATTCTAACATCTCTGAAGACTCATTCTCTA
GATTCAAGCAAACCAACACCCATTATGGTGGAAAGCCTCTAACAGCCCGTACCCAGCG
GGTTTCTGTTGAAGATCGTAAATCAAACACTGAACGCTGACGCTTTCTCTGTCACACAGAACT
TTTCCCTACTGCTTCTAGTGGCATTATACCCCTATGATTTCAAGGGGATTATGTTGACCAATTCAAG
TATGACAATCATGTGCCGACACCGCTGATGGCAATAACCACATCACAAGGCTGGTGGGGCTTCCTGGTGC
CGTTTTCATCATGGTAATTGTTACAGCCTCATCGTCTTCAGAATGCGAAAACCAACTCACCAAGTC
TCGGAACAAAACCTTCGGGGCTGTGGCTGTGGTCACTGCTTTTATCTGCTGGACTCCATACCAT
CTTGTGGAGTCCTGCTATTGATTACTGATCCAGAAAGTCCTGGGGAGCTGTGATGTCCTGGGACC
ACATGTCATTGCTTAGCATCTGCCATTGCAATAGTGTCTAACCTTCTGTATGCCCTTGGGGAAAGA
CTTTAGGAAGAACGAGACAGTCTATAAGGGATTCTGGAGCAGCCTTCAGCGAAGAGCTCACGCAC
TCTACCAACTGTACCCAGACAGCCTTCAAAAAGAACATATGAGTACAGATGTGAAAGATGTG
GCCCTGGGAACCTAACGAGGTTCTCAGGTGAAACAGTGTGACATGTGAGCAGGACACTTAGACA
ATTTGGGACTCTCAGAGAAAGGTCTTATTGACATCAGCATCATTGAAAACATTAAAGATGCAAAT
TTCAAGCCCCATCCCAGATGTGTTGACTCAGAATCTCTGGCCATGGGACCACTGTTTAACAGGCCCTC
TTGTTTCCATCAGTGTAAAGTTTACCTCATTGGCTTAGTCATTCCATCCCTGACTACACCATGTGC
AATGAATAACTTTTCACTGTTTCAGTATTCTTTCTTAGCATCATCTAAACTCTAGTTG
CATGGAGGCTGCTTATTGTTCTGAATGGAAGATATTCAATTATTGACAGTTGTGGTGGTGAACAA
GTGATTTTAAGTGGGAAAGAGACACAGTAAGAAAAGATCTATGAAAGCAGGGAGTGTGAGTTAGAGT
TTGACAGAACACAGTGCCAATGCCACCAACTAAAGCAACCTGAGATAATTCCAGTGTGAGC
AGTGAGCACAGATAACACACTTCCTACTCCTGGAGTGTAGTTAGAAGTTGTAGCTGGAGCTC
(SEQ ID NO:1)

MESFDADTNSTDLSRPLFQPQDIASMVLGLTCLLGLNGLVLWAGVKMKTTVNTVWFHLHT
LADFLCCLSLPFSLAHLILQGHWPYGLFLCKLIPSIILNMFAVFLLTAISLDRCIIVHKPIWCQNHR
NVRTAFAICGVVVAFVMCPVFYRDLFIMDNRSCRYNFDSRSYDYWDYVYKLSLPESNS
TDNSTAQLTGHMNDRSAPSSVQARDYFWTVTTALQSQPFLTSPEDSFSLDSANQQPHYGGKPP
NVLTAAPSGFPVEDRKSNTLNADAFLSAHTELFPTASSGHLYPYDFQGDYVDQFTYDNHVPTP
LMAITITRLVVGFLVPFFIMVICYSLIVFRMRKTFRVAVAVTVFFICWTPYHLGVLL
LITDPESSLGEAVMSWDHMSIALASANSFCNPFLYALLGKDFRKARQSIKGILEAAFSEELTHST
NCTQDKASSKRNNMSTDV (SEQ ID NO:2)

FIG. 1

underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

AGGGAGAGTCTGCCACAAGTTTGATATTTCACTGAGGCATCTATTCAAGTTGG
GCAGCAGACACTGAGCAGAACGTAGCACGGCAATGCTGGTAGCAATGCCTGTCCGGCA
GCACTCAGAAGACGGAGGAGAATCATAGCTTCAGTCAGCCTCTACAATATAG
TCAGTTGGAAGTCAGCAGCTAGACAACATGGAGAGCCTGT [GCCAAAGCCACTGGGT]
AGCCCGAATCTCAGTACAGAGAGCTGCCAGGGTGCCTACTGC :AAAAAAAAACCTCA
ACAACAGAAGTAGGGAGGTGTAAAAATAAGTGTAGGGGGTGGAAATTAAAGCTGATGTG
GACTTCAAATAAAAGTTACCTTAGATACTATTAAATCAATAGCATAGACCTGAAAC
TGTCTATCAGAAAATGTGTCTATTCTGAGGAAGGAGTGTCTAACGAGGTTCTGTGAGGGGG
GCCTCTGGCTTGGAGAGGGTGTACCATCACATAAGACTCCTAAAGCACATACTTTATA
AATTCAACATGAGCTTAAACATCTCTTGTCACTTCGAGACTGAGCCATGGAGTCTT
CGATGCTGACACCAATTCAACTGACCTACACTCACGGCCTCTGTTCAACCCAAGACAT
TG] CCTCCATGGTCAATTGGTCACTTGTCTATTGGGACTGCTAGGCAATGGGCTGGT
GCTGTGGTAGCTGGCGTAAAGATGAAGACGACCGTGAACACAGTCTGGTTCCATCT
CACCCCTGGCGATTTCTCTGCTGCCTCTCCCTGGCTCACCTGATTCT
CCAAGGACACTGGCCAT [GGCTTGTTCCTGTGCAAACCTATCCCATCCATCATTATTCT
CAACATGTTGCCAGTGTCTCCGTCTACTGCCATTAGCCTGGACCGATGTCTGATAGT
ACATAAGCCAATCTGGTCCAGAACATCGAAACGTGAGAACCGCCTCGCCATCTGTGG
ATGTGTCTGGTGGTAGCCTTGTGATGTGTGCCCCATTGTATACCGTGATCTGTT
CATTATGGACAATCGCAGTATATGTAGATATAATTGATTCTCCAGGTCAATGATTA
TTGGGACTACGTGT] ACAAAACTAAGTCTACCAGAAAGCAATTCTACTGATAACTCCACTGC
TCAGCTAACTGGACATATGAATGACAGGTCACTCCCTCTGTACAGGCAAGGGATTA
CTTTTGGACAGTTACCACTGCCCTCCAGTCACAGGCCATTCTAACATCTCTGAAGACTC
ATTCTCTCTAGATTCAAGCAACCAACCAACCCATTATGGTGGAAAGCCTCTAACATGCTC
CACAGCCGCCGTACCCAGCGGGTTCTGTGAAGATCGTAAATCCAATACACTGAACGC
TGACGCTTTCTCTGTCACACAGAACTTTCCCTACTGCTCTAGTGGTCATTATA
CCCCTATGATTCCAGGGGGATTATGTTGACCAATTCACTGATGACAATCATGTGCCGAC
ACCGCTGATGGCAATAACCATCACAAGGCTGGTGGCTTCCTGGTGCCTTTTCAT
CATGGTAATTGTTACAGCCTCATGTCTCAGAATGCGAAAACCAACTTCACCAAGTC
TCGGAAACAAAACCTCGGGTGGCTGTGGCTGTGGTCACTGTCTTTTATCTGCTGGAC
TCCATACCCTTGTGCGAGTCCTGCTATTGATTACTGATCCAGAAAGTTCTGGGGAA
AGCTGTGATGTCCTGGGACCACATGTCCATTGCTTAGCATCTGCCAATAGTTGCTTCAA
CCCTTCTGTATGCCCTTGGGAAAGACTTTAGGAAGAAGCAAGACAGTCTATAAA
GGGCATTCTGGAAGCAGCCTTCAGCGAAGAGCTCACGCACACTTACCAACTGTACCCAAAGA
CAAAGCCTTCAAAAAGAAACAATATGACTACAGATGTGTGAAGATGTGCCCTGGGAA
CCTAAGCAGAGTTCTCAGGTGAACAGTGATGGATGACATGTGAGCAGGACACTTAGACA
ATTGGCGACTCTCAGAGAAAGGTCTTATTGACATCAGCATCTTGAAACATTTAA
GATGCAAATTCAGCCCCATCCCAGATGTGTTGACTCAGAATCTCTGCCCATGGAC
CAGTGTAAACAGGCCCTTGTGTTCCATCAGTGTAAAGTTACCTCATTTGCTTAG
TCTATTCCCATCCCTGACTACACCATGTGCAATGAATACTTTTCTGTTTGTGCTTA
TTCTTTTTCTTAGCATCATCTAAACTCTAGTTGCTGATGGAAGGCTGCTCTTATT
GTTCTGAATGGAAGATATTCAATTGACAGTTGTTGAGCTGAGTTAGAGT
AGTGGGAAAGAGACACAGTAAGAAAAGATCTATGAAAGCAGGGAGTGTGAGTTAGAGT
TTGACAGAACACAGTGCCAAATGCCACCCACTAAAAGCAACCTGAGATAATTCCAGTGT
CATGTGAGCAAGTGAGCACAGATAACACATAAAACACTTCCCTACTCCTGGAGTGTAG
AGTTGTAGCTGGAGCTC

FIG. 2A

Gene Sequence
Structure *

663 bp

Sequence Deleted

859 bp

Size of full-length
cDNA: 2658 bp

Targeting Vector* (genomic sequence)

Construct Number: 3036

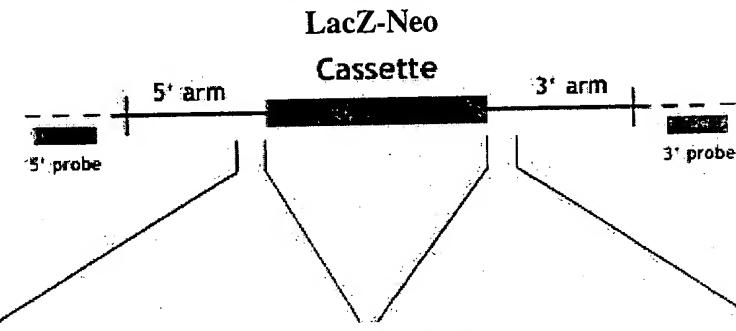
Arm Length:

5': 3.2 kb

3': 1.8 kb

Targeting Vector
Endogenous Locus

Not drawn to scale

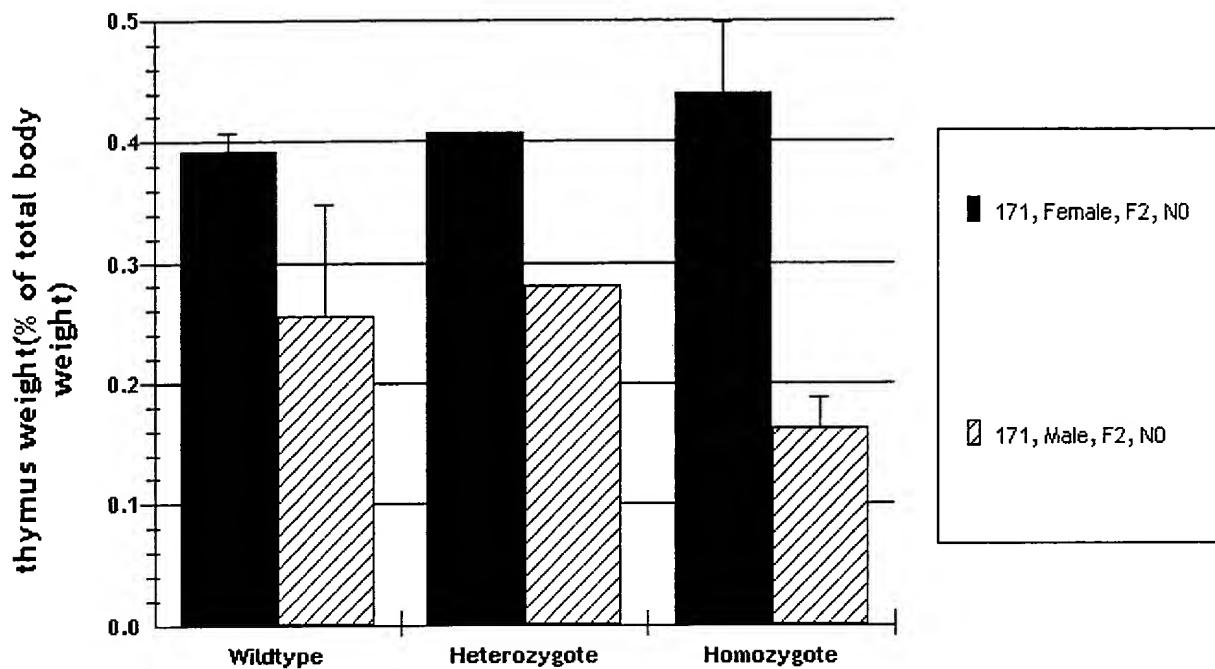


5' >CGAGGTTCTGTGAGGGGGCC
TCTGGCTTGAGAGGGTGTACCAT
CACATAAGACTCCTAAAAGCACAT
ACTTTTATAAATTCAACCAGAGCT
TTAACATCTTGTCAATTTCGC
AGACTGAGCCATGGAGTCTTCGA
TGCTGACACCAATCAACTGACCT
ACACTCACGGCCTCTGTTCAACC
CCAAGACATTG<3' (SEQ ID
NO: 3)

5' >GGCTTGTCTGTGCAAACCT
ATCCCATCCATCATTATTCTCAAC
ATGTTGCCAGTGTCTCCTGCTT
ACTGCCATTAGCCTGGACCGATGT
CTGATAGTACATAAGCCAATCTGG
TGCCAGAACATCGAAACGTGAGA
ACCGCCTTCGCCATCTGTGGATGT
GTCTGGGTGGTAGCCTTGTGATG
TGTGTGCCGT<3' (SEQ ID
NO: 4)

FIG. 2B

necropsy - thymus weight/body weight



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Fig. 3